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Dietary Exposure of Mink to Carp from Saginaw Bay. 3. Characterization of Dietary Exposure to Planar Halogenated Hydrocarbons, Dioxin Equivalents, and Biomagnification

DONALD E. TILLITT,*,†
ROBERT W. GALE,†
JOHN C. MEADOWS,†
JAMES L. ZAJICEK,†
PAUL H. PETERMAN,†
SILVIA N. HEATON,‡ PAUL D. JONES,§
STEVEN J. BURSIAN,‡
TIMOTHY J. KUBIAK,∥
JOHN P. GIESY,⊥ AND
RICHARD J. AULERICH‡

National Biological Service, Midwest Science Center, 4200 New Haven Road, Columbia, Missouri 65201, Department of Animal Science, Michigan State University, East Lansing, Michigan 48824, Wellington Science Center, ESR Environmental, Gracefield, P.O. Box 30547, Lower Hutt, New Zealand, U.S. Fish and Wildlife Service, Division of Environmental Contaminants, 4401 North Fairfax Drive, No. 330, Arlington, Virginia 22203, and Department of Fisheries and Wildlife, Pesticide Research Center, Institute for Environmental Toxicology, Michigan State University, East Lansing, Michigan 48824

Mink are known to be very sensitive to the toxic effects of planar polychlorinated biphenyls (pPCBs), polychlorinated dibenzo-*p*-dioxins (PCDDs), and polychlorinated dibenzofurans (PCDFs), collectively known as planar halogenated hydrocarbons (PHHs). Previously, we reported the reproductive effects in mink fed a diet containing 10, 20, or 40% fish taken from Saginaw Bay, Lake Huron. The present study reports the chemical characterization of the diets and the adult mink livers, along with a comparison of an additive model of toxicity with the results of the H4IIE bioassay on these samples. The assessment of dietary or tissue-based exposure of the mink to 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD) and related compounds revealed that TCDD equivalents of the PHH mixtures largely followed an additive model of toxicity as compared with the H4IIE bioassay. Consistent dietary and liver tissue-based threshold concentrations for reproductive toxicity in mink were determined regardless of whether PHHs were quantified as TEQs (additive toxicity) or TCDD-EQs (H4IIE bioassay). Significant reproductive effects were observed in the lowest treatment group (10% fish or 19.4 pg of H4IIE bioassay-derived TCDD-EQs/g). Consumption-normalized mink liver biomagnification factors (BMFs) were 6.4–74.2 for PCDDs, <1–75.8 for PCDFs, <1–15.9 for PCBs, and in general, increased with degree of chlorination within each class. Based on TEQs or TCDD-EQ, this study confirms that mink are among the most, if not the most, sensitive mammalian species to the reproductive toxicity of TCDD and related compounds.

Introduction

The Great Lakes of North America as well as other areas of the world have been contaminanted with toxic, persistent, and bioaccumulative chemicals. One such class of chemicals consists of planar polychlorinated biphenyls (pPCBs), polychlorinated dibenzo-*p*-dioxins (PCDDs), and polychlorinated dibenzofurans (PCDFs), collectively known as planar halogenated hydrocarbons (PHHs). The prototypic and most potent PHH is 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (TCDD). PHHs exert their toxic effects of reduced body weight gain, thymic atrophy, immune suppression, and reproductive toxicity through a cytosolic receptor, the aryl hydrocarbon receptor (Ah-R; *1, 2*) that is present in vertebrates beginning with cartilaginous fishes (*3*). Evidence of PHH poisoning in the environment has been demonstrated in both fish and wildlife species (*4–9*). The most severe effects have been observed in species at the top of the food web which receive the greatest doses of PHHs.

Mink (*Mustela vison*) are top carnivores in aquatic ecosystems and are particularly sensitive to the effects of PHHs (*10*). Their sensitivity to PHHs is similar to that of the most sensitive species tested in acute laboratory toxicity studies, the guinea pig (*11*). The LD50 of TCDD in mink, based on a single oral dose, was 4.2 μg/Kg body weight (*12*). Mink are also sensitive to the reproductive toxicity of PHHs. Numerous laboratory feeding studies have demonstrated that mink reproduction is disrupted by small amounts of dietary PHHs either as commercial mixtures or pure compounds (*10, 13–17*) or when added to their diet in the form of contaminated fish (*18–21*). Reduced numbers of females whelping, reduced litter sizes, and excessive kit mortality at birth and at 6 weeks of age have been observed effects of PHHs in the diets of mink. The dietary threshold concentrations for these reproductive effects in mink are near and, in some situations, considerably less than the concentrations of PHHs that are observed in fish from contaminated areas (*21*).

PHHs exist in the environment as complex mixtures of chemicals that change relative patterns according to the sources of the contamination, environmental fate char-

* Corresponding author telephone: 314-875-5399 (ext. 1886); fax: 314-876-1896; e-mail address: donald_tillitt@nbs.gov.
† National Biological Service.
‡ Michigan State University.
§ ESR Environmental.
∥ U.S. Fish and Wildlife Service.
⊥ Institute for Environmental Toxicology.

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acteristics, and the toxicokinetics of the PHHs in individual species (*22*). Moreover, individual PHHs that compose the complex mixtures found in the environment exhibit large differences in their relative toxic potencies (*11*). An additive model of toxicity is currently used to assess the potential toxicity of PHH mixtures (*23–24*). Potencies of individual PHHs are normalized to that of TCDD based on their median values of toxicity for various end points (enzyme induction, thymic atrophy, immune suppression, embryo or fetal lethality, etc.) and expressed as toxic equivalency factors (TEFs). TEFs are fractional potencies used in exposure assessment to estimate TCDD toxic equivalents (TEQs) based on the sum of TEF-normalized PHH concentrations. The concentrations of PHHs are multiplied by their TEF values, and the resultant TCDD-normalized concentrations for all the measured analytes are summed in an additive model to attain total TEQs in the sample. Although additivity appears to be the general rule for PHH toxicity, nonadditive effects and modulation of PHH toxicity by non-PHH compounds occur (*11*). For these reasons, an *in vitro* bioassay has been proposed as an integrative measure of PHHs for exposure assessment of environmental samples (*25, 26*).

In this study, we exposed mink to various amounts of carp (*Cyprinus carpio*) collected from Saginaw Bay, Lake Huron, MI, and observed the reproductive effects. The details of the reproductive effects were given in earlier reports (*21, 27*). In this portion of the study, quantification of the dioxin-like activity was estimated by two different methods. One method was based on the relative potencies (TEF values) of individual PHH compounds and an additive model of toxicity to give TEQs. The other method utilized an *in vitro* bioassay of the complex mixtures of PHHs found in the samples to directly quantify dioxin-like potency and is reported as TCDD-EQ. We conducted this study to calibrate the H4IIE bioassay TCDD-EQ from an environmentally weathered PHH mixture to ecologically relevant end points in a sensitive species that occurs in the Great Lakes region.

The objectives of the present study were to (1) characterize the dietary exposure of the mink to PHHs; (2) compare an additive model of PHH toxicity (TEQs) with TCDD equivalents derived from the H4IIE bioassay (TCDD-EQs); (3) validate the use of the H4IIE bioassay for use in mink; (4) assess the effect of these methods on the calculation of an estimated threshold dose (ETD) for reproductive toxicity in mink; and 4) determine biomagnification factors (BMFs) for PHHs from diets to mink livers which may be used in field risk assessments.

Experimental Section

Mink Exposure. Carp were collected by electrofishing in Saginaw Bay, MI, near the mouth of the Saginaw River on December 2, 1988. Details of the preparation of diets and subsequent exposure of the mink were presented in Heaton et al. (*21*). Briefly, dietary exposures were 0, 10, 20, or 40% ground, cooked, Saginaw Bay carp mixed into a standard mink ration and fed *ad libitum*. Each treatment group contained 3 males and 12 females. Dietary exposures began approximatley 52 days prior to breeding and 104 days prior to whelping of the kits. Feed consumption and body weights of females were monitored weekly through the first 12 weeks of the trial. The study was continued until the kits were approximately 6 weeks old (day 182 of exposure), at which time all remaining adult female mink were euthanized and necropsied. Livers were subsampled for biochemical and chemical analysis.

H4IIE Bioassay and TEFs. Extracts of the composite diets and individual livers were prepared and tested with the H4IIE bioassay as previously described (*26*). H4IIE bioassay-derived TCDD equivalents (TCDD-EQ) were determined by comparison of ethoxyresorufin *O*-deethylase (EROD) induction in the extract-treated cells with EROD induction in TCDD-treated cells (*26*). The H4IIE TEF values are those derived from testing in the bioassay (*26, 28, 29*; and unpublished data). The TEF values developed for risk assessment, international TEFs (I-TEFs), were arrived at through consensus of a wide variety of toxic end points and species (*23, 24*). Concentrations of PHHs in the diets and livers of mink were multiplied by their TEF value (both H4IIE TEFs and I-TEFs were evaluated) to obtain TCDD equivalents (TEQs) from the chemical analysis. Concentrations less than detection limits were set to zero for the determination of TEQs.

Chemical Analysis. Time-weighted composites of diets (based on the amount of time the mink were fed various batches of the diets) and composite samples of livers from adult females were analyzed for PCDDs, PCDFs, and PCBs. Preparation of the samples included drying homogenates with sodium sulfate, extraction with dichloromethane, gravimetric lipid determination, reactive cleanup, gel permeation chromatography, and fractionation by carbon high-pressure liquid chromatography (HPLC) as described previously (*30*). The analytes were separated into four discrete fractions by dual HPLC columns of carbon dispersed on C_{18}: (1) bulk and di-ortho-substituted PCBs; (2) non-ortho-substituted PCB's (3) PCDDs and PCDFs; and (4) mono-ortho-substituted PCBs (*30*). Prior to extraction, each sample was spiked with ^{13}C-labeled recovery standards for the non-ortho-substituted PCBs, PCDDs, and PCDFs. Analytes in fractions 1 and 4 were determined by capillary gas chromatography (GC) with electron capture detection (GC-ECD, *31*), analytes in fraction 2 of the diets were determined by GC/high-resolution mass spectrometry (HRMS) by modifications of the methods of Kuehl et al. (*32*), while analytes in fraction 2 from the liver samples were analyzed by GC-ECD and analytes in fraction 3 were determined by low-resolution mass spectrometry (LRMS). Due to the large amounts of 2,3,4,7,8- pentachlorodibenzofuran (2,3,4,7,8-PCDF) found in the diets and subsequently in the mink livers, confirmational analysis was performed by GC-LRMS using a 60 m × 250 μm SP-2331 capillary column based on its ability to completely resolve 2,3,4,7,8-PCDF from other penta-CDF congeners (*33*).

Biomagnification Factors (BMFs). Mink liver BMFs were determined for all PHHs based on lipid-normalized analyte concentrations according to eqs 1 and 2:

$$\nu_l = (\alpha C/K)\nu_d\,(1 - e^{-Kt}) \qquad (1)$$

or

$$\mathrm{BMF} = \nu_l/\nu_d = (\alpha C/K)\,(1 - e^{-Kt}) \qquad (2)$$

where ν_l is the lipid-normalized concentration in the liver (pg/g); α is the assimilation efficiency of uptake; C is the consumption rate (g of food (g of body wt)$^{-1}$ d^{-1}); K is the total loss rate constant (d^{-1}); ν_d is the lipid-normalized dietary concentration (pg/g); and t is the time (d). If it is assumed that K is a constant across treatment groups, then

TABLE 1

Concentrations (pg/g) of PCDDs, PCDFs, and PCBs in Raw and Cooked Saginaw Bay Carp and Diets Fed to Mink[a]

	Saginaw Bay Carp (n = 3)		diet (n = 2)			
compound	raw	cooked	control	10% carp	20% carp	40% carp
2,3,7,8-TCDD	21 (0.6)	20 (0.6)	ND[b]	2 (0.0)	3 (1.4)	7 (1.4)
1,2,3,7,8-PECDD	12 (0.0)	12 (0.0)	ND	2 (0.0)	2 (0.0)	4 (0.0)
1,2,3,4,7,8-HXDD	4 (0.0)	4 (0.6)	ND	2 (1.4)	1 (0.7)	3 (0.7)
1,2,3,6,7,8-HXCDD	17 (0.6)	18 (0.6)	ND	1 (0.7)	3 (1.4)	6 (0.0)
1,2,3,7,8,9-HXCDD	2 (0.0)	1 (1.1)	ND	1 (0.7)	1 (0.7)	1 (0.0)
1,2,3,4,6,7,8-HPCDD	19 (1.1)	19 (0.0)	5 (1.4)	7 (1.4)	6 (2.8)	13 (0.7)
OCDD	15 (1.5)	17 (1.1)	37 (3.5)	45 (1.4)	30 (14)	50 (2.8)
2,3,7,8-TCDF	35 (1.1)	34 (0.5)	ND	2 (0.7)	4 (2.8)	12 (0.7)
1,2,3,7,8-PECDF	15 (1.1)	15 (0.6)	ND	1 (0.0)	2 (0.7)	4 (0.7)
2,3,4,7,8-PECDF	41 (2.3)	41 (1.0)	ND	4 (0.7)	6 (2.8)	14 (0.0)
1,2,3,4,7,8-HXCDF	9 (1.1)	11 (1.1)	ND	1 (0.0)	2 (0.7)	3 (0.0)
1,2,3,6,7,8-HXCDF	6 (0.0)	5 (1.1)	ND	1 (0.0)	1 (0.0)	2 (0.0)
1,2,3,7,8,9-HXCDF	ND	ND	ND	ND	ND	ND
2,3,4,6,7,8-HXCDF	6 (0.6)	7 (1.1)	ND	1 (0.7)	2 (0.7)	2 (0.0)
1,2,3,4,6,7,8-HPCDF	11 (1.1)	11 (1.1)	ND	2 (0.0)	3 (1.4)	5 (0.7)
1,2,3,4,7,8,9-HPCDF	ND	ND	ND	ND	ND	ND
OCDF	1 (0.6)	1 (0.6)	1 (0.0)	1 (0.1)	1 (0.0)	1 (0.7)
3,4,4',5-TCB (81)	320 (70)	320	2	27	66	150
3,3',4,4'-TCB (77)	1500 (180)	1400	11	300	600	1100
3,3',4,4',5-PECB (126)	660 (160)	540	5	88	210	410
3,3',4,4',5,5'-HXCB (169)	70 (30)	60	2	5	10	20
2',3,4,4',5-PECB (123)	6900 (1000)	*c*	30	920 (160)	1690 (160)	3270 (180)
2,3',4,4',5-PECB (118)	262000 (60000)	*c*	1660	35000 (8100)	68000 (280)	125000 (9800)
2,3,4,4',5-PECB (114)	9100 (2700)	*c*	30	1200 (310)	2400 (100)	4700 (440)
2,3,3',4,4'-PECB (105)	87900 (19000)	*c*	510	12000 (2800)	23000 (750)	41000 (3100)
2,3',4,4',5,5'-HXCB (167)	8500 (1800)	*c*	110	1100 (280)	2200 (70)	4000 (350)
2,3,3',4,4',5-HXCB (156)	9600 (3000)	*c*	110	1300 (210)	2800 (280)	5000 (350)
2,3,3',4,4',5'-HXCB (157)	1860 (530)	*c*	40	280 (60)	540 (20)	940 (70)
2,3,3',4,4'5,5'-HXCB (189)	1300 (760)	*c*	10	200 (60)	410 (0)	740 (60)
total PCBs (μg/g)	8.40 (1.44)	*c*	0.015	0.72	1.53	2.56

[a] Concentrations followed by standard deviation (n = 3) or relative difference (n = 2). n = 1 for values without parentheses. Concentrations of PCDDs and PCDFs in cooked and raw carp were not significantly different from one another (Tukey's test, $p < 0.05$). [b] ND, not determined. [c] Samples compromised during processing. Detection limits were <1.0 pg/g for PCDDs, PCDFs, and non-ortho-substituted PCBs and <100 pg/g for mono-ortho-substituted PCBs.

the BMF is directly proportional to the consumption rate as

$$\mathrm{BMF} = \mathrm{BMF}_t\,(C_a/C_t) \qquad (3)$$

where BMF_t is the treatment BMF based on lipid-normalized concentration ratio in eq 2; C_a is the estimated average year-round consumption rate for mink (*34*); and C_t is the consumption rate of treatment group (g of food (g of mink)$^{-1}$ d^{-1}).

Statistical Analysis. Comparisons among treatment groups were made by one-way analysis of variance (ANOVA), and differences among treatment means and PHH concentrations in cooked and raw carp were tested with Tukey's test ($p < 0.05$; *35*).

Results and Discussion

Concentrations of PHHs, TEQs, and TCDD-EQs in the Diets. PCBs, PCDDs, and PCDFs were detected in the Saginaw Bay carp collected in December 1988 at the mouth of the Saginaw River (Table 1). Concentrations of PHHs in the steam-cooked carp, which was added to the mink diets (cooked to deactivate thiaminase activity), did not differ from those measured in the raw carp (Table 1). Concentrations of PHHs in the treatment diets were consistent with the portions of Saginaw Bay carp added to the diets (Table 1). Concentrations of PCDD and PCDFs in the control diet (40% ocean fish) were below detection limits except for small amounts of 1,2,3,4,6,7,8-heptachlorodibenzo-*p*-dioxin (1,2,3,4,6,7,8-HpCDD), octachlorodibenzo-*p*-dioxin (OCDD), and octachlorodibenzofuran (OCDF). Small but measurable amounts of PCBs (0.015 μg/g) were also found in the control diet.

Concentrations of PHHs in the diets and TEFs derived from the H4IIE bioassay (TEQs) were used to calculate total dioxin-like exposure from these chemicals (Table 2). The percent contribution of PCDDs, PCDFs, non-ortho-PCBs, and mono-ortho-PCBs to the total TEQs in the treatment group diets averaged 22.4 ± 2.8%, 55.9 ± 1.2%, 20.0 ± 3.8%, and 0.4 ± 0.2%, respectively. Dietary exposures of mink to the PHHs in the various treatment groups were estimated based on food consumption by individual mink (Table 3).

The H4IIE bioassay of Ah-R agonists has long been used as an integrative assay for the toxicological assessment of PHH mixtures (*25, 26, 36*). H4IIE bioassay-derived TCDD-EQs of synthetic mixtures of PHHs have demonstrated additive responses as compared to TEQs (*36*). However, in environmental samples in which PCDDs, PCDFs, and pPCBs have been measured, the limited amount of data has indicated that the H4IIE bioassay-derived TCDD-EQs are greater (approximately 60%) than TEQs estimated in the same samples (*37*). A similar ratio of TEQs to TCDD-EQs was observed in the diet samples in this study (Table 2). H4IIE TCDD-EQs in the diets were consistently greater

TABLE 2

Concentrations (pg/g) of TCDD Toxic Equivalents (TEQs) and H4IIE Bioassay-Derived TCDD Equivalents (TCDD-EQ) in Diets Fed to Mink

compound	H4IIE TEF[a]	diet			
		control	10% carp	20% carp	40% carp
2,3,7,8-TCDD	1.000 000	0.0	2.0	3.0	7.0
1,2,3,7,8-PECDD	0.420 000	0.0	0.8	0.8	1.7
1,2,3,4,7,8-HXCDD	0.083 000	0.0	0.2	0.1	0.2
1,2,3,6,7,8-HXCDD	0.024 000	0.0	0.0	0.1	0.1
1,2,3,7,8,9-HXCDD	0.034 000	0.0	0.0	0.0	0.0
1,2,3,4,6,7,8-HPCDD	0.023 000	0.1	0.2	0.1	0.3
OCDD	0.000 504	0.0	0.0	0.0	0.0
total PCDD TEOs		0.1	3.2	4.2	9.4
% total		51.4	25.7	20.4	21.2
2,3,7,8-TCDF	0.200 000	0.0	0.4	0.8	2.4
1,2,3,7,8-PECDF	0.200 000	0.0	0.2	0.4	0.8
2,3,4,7,8-PECDF	1.400 000	0.0	5.6	8.4	19.6
1,2,3,4,7,8-HXCDF	0.020 000	0.0	0.0	0.0	0.1
1,2,3,6,7,8-HXCDF	0.060 000	0.0	0.1	0.1	0.1
1,2,3,7,8,9-HXCDF	0.200 000	0.0	0.0	0.0	0.0
2,3,4,6,7,8-HXCDF	0.300 000	0.0	0.3	0.6	0.6
1,2,3,4,6,7,8-HPCDF	0.300 000	0.0	0.6	0.9	1.5
1,2,3,4,7,8,9-HPCDF	0.020 000	0.0	0.0	0.0	0.0
OCDF	NA[b]	0.0	0.0	0.0	0.0
total PCDF TEOs		0.0	7.2	11.2	25.1
% total		0.0	56.9	54.5	56.3
3,4,4′,5-TCB (81)	0.001 900	0.00	0.05	0.13	0.29
3,3′,4,4′-TCB (77)	0.000 018	0.00	0.01	0.01	0.02
3,3′,4,4′,5-PECB (126)	0.022 000	0.11	1.94	4.62	9.02
3,3′,4,4′,5,5′-HXCB (169)	0.000 470	0.00	0.00	0.00	0.01
total non-ortho-PCB TEOs		0.1	2.0	4.8	9.3
% total		43.8	15.8	23.2	20.9
2′,3,4,4′,5-PECB (123)	0.000 012	0.00	0.01	0.02	0.04
2,3′,4,4′,5-PECB (118)	0.000 000 35	0.00	0.01	0.02	0.04
2,3,4,4′,5-PECB (114)	<0.000 001	0.00	0.00	0.00	0.00
2,3,3′,4,4′-PECB (105)	0.000 008	0.00	0.09	0.17	0.31
2,3′,4,4′,5,5′-HXCB (167)	0.000 009	0.00	0.01	0.02	0.04
2,3,3′,4,4′,5-HXCB (156)	0.000 055	0.01	0.07	0.15	0.28
2,3,3′,4,4′,5′-HXCB (157)	0.000 015	0.00	0.00	0.01	0.01
2,3,3′,4,4′,5,5′-HXCB (189)	0.000 010	0.00	0.00	0.00	0.01
total mono-ortho-PCB TEOs		0.0	0.2	0.4	0.7
% total		4.8	1.6	2.0	1.6
grand total TEOs (pg/g)		0.3	12.6	20.5	44.6
H4IIE TCDD-EOs (pg/g)		1.0	19.4	40.0	80.8

[a] H4IIE TEF values from Tillitt et al. (*26, 28*); Tysklind et al. (*29*); or unpublished values. [b] NA, not active in H4IIE bioassay.

TABLE 3

Dietary Exposure of Mink Fed Various Percentages of Carp from Saginaw Bay, Lake Huron, MI[a]

	diets			
	control	10% carp	20% carp	40% carp
12-week cumulative feed consumption (g/mink)	22,317 (711)	18,319 (614)	16,508 (522)	12,622 (750)
dietary TEQ concn (pg/g)	0.3	12.6	20.5	44.6
dietary H4IIE TCDD-EQ concn (pg/g)	1	19.4	40	80.8
cumulative TEQ dose (ng/mink)[b]	6.6 (0.2)	231 (7.7)	338 (10.7)	563 (33.5)
cumulative H4IIE TCDD-EQ dose (ng/mink)[b]	22.3 (0.73)	355.4 (11.8)	660.3 (20.1)	1019.9 (60.6)
ng of TEQ mink^{-1} day^{-1} [b]	0.08 (.002)	2.75 (0.09)	4.02 (0.13)	6.70 (0.40)
ng of H4IIE TCDD-EQ mink^{-1} day^{-1} [b]	0.27 (0.07)	4.23 (0.26)	7.86 (0.26)	12.14 (0.46)
ng of TEQ (kg of body wt)$^{-1}$ day^{-1} [b]	0.08 (.002)	2.24 (0.07)	3.50 (0.01)	5.36 (0.32)
ng of H4IIE TCDD-EQ (kg of body wt)$^{-1}$ day^{-1} [b]	0.27 (0.01)	3.44 (0.11)	6.84 (1,98)	9.71 (0.45)

[a] Mean values followed by standard error of the mean in parentheses. [b] Each dietary value is significantly different from the others in the row ($p < 0.05$).

than the TEQs based on concentrations of PHHs. The TEQs, which were calculated using H4IIE TEF values, were 57 ± 7.6% of the H4IIE TCDD-EQ measured in the diets by bioassay (Table 2). The differences between these two measures of Ah-R potency could have been due to synergism of compounds present in the mixtures, the accuracy and precision of the measurements, or the fact that there were Ah-R active compounds present in the mixture that were not measured yet contributed to the dioxin-like potency of the mixture.

TABLE 4

Liver Concentrations (pg/g) of PCDDs, PCDFs, PCBs, and TEQs in Mink Fed Diets Containing Carp from Saginaw Bay, Lake Huron, MI[a]

	liver PHH concn (pg/g)				liver toxic equivalents (TEQs, pg/g)			
	diet				diet			
compound	control	10% carp	20% carp	40% carp	control	10% carp	20% carp	40% carp
2,3,7,8-TCDD	1 (0.7)	21 (1.4)	34 (3.5)	50 (3.5)	1.0	21.0	34.0	50.0
1,2,3,7,8-PECDD	ND	7 (0.7)	10 (0.7)	17 (0.7)	0.1	2.9	4.2	7.1
1,2,3,4,7,8-HXCDD	ND	6 (3.5)	10 (0.7)	15 (1.4)	0.0	0.5	0.8	1.2
1,2,3,6,7,8-HXCDD	8 (0.0)	54 (2.1)	77 (7.1)	130 (0.0)	0.2	1.3	1.8	3.1
1,2,3,7,8,9-HXCDD	3 (1.4)	8 (0.7)	8 (0.7)	10 (0.0)	0.1	0.3	0.3	0.3
1,2,3,4,6,7,8-HPCDD	115 (7.1)	330 (28)	290 (35)	380 (28)	2.6	7.6	6.7	8.7
OCDD	490 (14.1)	2200 (640)	1900 (490)	2400 (570)	0.3	1.2	1.0	1.3
total PCDD TEQs					4.3	34.8	48.8	72.0
% total					38.9	10.7	8.5	8.0
2,3,7,8-TCDF	ND	2 (2.1)	2 (0.7)	3 (0.0)	0.0	0.4	0.4	0.6
1,2,3,7,8-PECDF	ND	1 (0.7)	2 (0.0)	2 (2.1)	0.0	0.2	0.4	0.4
2,3,4,7,8-PECDF	2 (1.4)	170 (21)	320 (57)	490 (71)	2.8	238.0	448.0	686.0
1,2,3,4,7,8-HXCDF	ND	33 (1.4)	73 (4.2)	130 (7.1)	0.0	0.7	1.5	2.6
1,2,3,6,7,8-HXCDF	ND	25 (0.7)	49 (2.1)	71 (1.4)	0.0	1.5	2.9	4.3
1,2,3,7,8,9-HXCDF	ND	ND	1 (0.7)	1 (0.7)	0.0	0.0	0.2	0.2
2,3,4,6,7,8-HXCDF	ND	37 (15)	60 (0.0)	98 (17)	0.0	11.1	18.0	29.4
1,2,3,4,6,7,8-HPCDF	4 (0.0)	33 (1.4)	58 (6.4)	89 (13)	1.2	9.9	17.4	26.7
1,2,3,4,7,8,9-HPCDF	ND	ND	1 (0.7)	2 (1.4)	0.0	0.0	0.0	0.0
OCDF	ND	34 (8.5)	15 (2.1)	28 ((4.2)	0.0	0.0	0.0	0.0
total PCDF TEQs					4.0	261.8	488.8	750.2
% total					36.2	80.7	84.6	83.5
3,4,4',5-TCB (81)	50 (0)	45 (7.1)	50 (0.0)	100 (14)	0.1	0.1	0.1	0.2
3,3',4,4'-TCB (77)	50 (0)	45 (7.1)	50 (0.0)	90 (0.0)	0.0	0.0	0.0	0.0
3,3',4,4',5-PECB (126)	115 (80)	1210 (130)	1700 (190)	3280 (50)	2.5	26.6	37.4	72.2
3,3',4,4',5,5'-HXCB (169)	65 (20)	65 (7.1)	120 (4.2)	205 (21)	0.0	0.0	0.1	0.1
total non-ortho-PCB TEQs					2.7	26.7	37.6	72.4
% total					24.1	8.2	6.5	8.1
2',3,4,4',5-PECB (123)	60 (0)	320 (35)	890 (140)	1760 (850)	0.0	0.0	0.0	0.0
2,3',4,4',5-PECB (118)	8500 (1200)	20000 (7700)	284000 (43000)	478000 (56000)	0.0	0.0	0.1	0.2
2,3,4,4',5-PECB (114)	170 (010)	4600 (360)	8400 (1500)	14400 (2100)	0.0	0.0	0.0	0.0
2,3,3',4,4'-PECB (105)	2900 (450)	54000 (3400)	105000 (17800)	181000 (22000)	0.0	0.4	0.8	1.4
2,3',4,4',5,5'-HXCB (167)	740 (160)	6400 (470)	11200 (2000)	18700 (3200)	0.0	0.1	0.1	0.2
2,3,3',4,4',5-HXCB (156)	920 (140)	12000 (610)	23000 (4000)	37100 (4500)	0.1	0.7	1.3	2.0
2,3,3',4,4',5'-HXCB (157)	340 (60)	3200 (200)	5700 (1100)	9360 (1290)	0.0	0.0	0.1	0.1
2,3,3',4,4',5,5'-HXCB (189)	100 (10)	1300 (90)	2700 (450)	4250 (780)	0.0	0.0	0.0	0.0
total mono-or tho-PCB TEQs					0.1	1.2	2.4	4.0
% total					0.8	0. 4	0.4	0.4
total PCBs (μg/g)	0.09 (0.02)	2.19 (0.73)	3.05 (2.02	6.27 (2.89)				
grand total TEQs (pg/g)					11	324	578	899
H4IIE TCDD-EQs (pg/g)		0.44			<10	495	439	656

[a] Concentrations followed by relative difference ($n = 2$). Detection limits were <1.0 pg/g for PCDDs and PCDFs; 30 pg/g for non-ortho-substituted PCBs; and <100 pg/g for the monoo-ortho-substituted PCBs.

Concentrations of PHHs, TEQs, and TCDD-EQs in the Mink Livers. PCDDs, PCDFs, and PCBs were found in the livers of mink from all of the treatment groups; however, many of the PCDFs and a few of the PCDDs were below detection in the livers of mink that were fed the control diet (Table 4). The calculated TEQs in composites of mink livers corresponded with the TCDD-EQs determined by the H4IIE bioassay in these samples (Table 4). The contribution of each PHH class to the total TEQs in mink livers was similar in all three of the carp treatment groups (Table 4), but slightly different than their contributions in the diets (Table 2). PCDDs were 8.0−10.7% ($\bar{x} = 9.1 \pm 1.4\%$), PCDFs were 80.7−84.6% ($\bar{x} = 83.0 \pm 2.0\%$), non-ortho-PCBs were 6.5−8.2% ($\bar{x} = 7.6 \pm 1.0\%$), and mono-ortho-PCBs were 0.4% ($\bar{x} = 0.4 \pm 0\%$) of the total TEQs in the mink livers (Table 4). Only the control livers had different contributions by the various groups of PHH compounds. This was due to small amounts and in some cases undetectable concentrations of analytes in the control livers.

TCDD-EQs in the mink livers were slightly lower than the TEQs estimated from PHH concentrations. The only exception to this was in the 10% carp treatment group (Table 4). The average concentration of TEQs in the livers of mink from the 10% carp treatment group was 65% that of the TCDD-EQs, similar to the observations in the diets (Table 2). The reason for these differences between TEQs and TCDD-EQs among diets and livers could be caused by several factors. One possible explanation for the difference is the relative ratios of Ah-R agonists to other compounds in the diets as compared to their relative ratios in the livers. Changes in PCB patterns across trophic levels due to differential metabolism and pharmacokinetics of the individual congeners have been demonstrated in birds (*22, 38*) and mammals (*39*). Selective accumulation and elimination of PCBs occurred in this study, as illustrated by GC-ECD chromatograms of a technical Aroclor mixture,

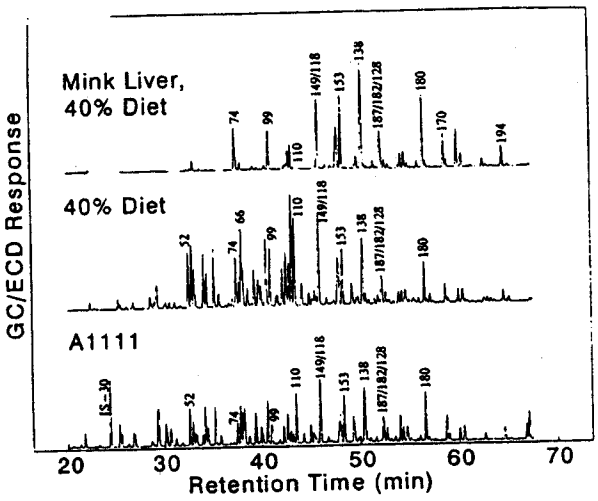

FIGURE 1. PCB chromatograms of an Aroclor standard (1:1:1:1 mixture, 1242:1248:1254:1260, 1 μg/mL of each), the composition of the 40% Saginaw Bay carp diet (2.5 g equivs/mL), and the livers of mink fed the 40% Saginaw Bay carp diet (0.73 g equivs/mL).

a 40% carp diet sample, and a liver sample from mink that were fed the 40% carp diet (Figure 1). Enrichment of selected PCB congeners with greater numbers of chlorines (later eluting) and specific losses of lower chlorinated PCB congeners (earlier eluting) were observed in the mink livers as compared to their diets (Figure 1). Clearly, the same type of selective losses or enrichments were observed with PCDD/PCDF congeners based on the BMFs (Table 5). Some of the PCB congeners that are selectively retained or enriched in the mink livers relative to their diets are not Ah-R agonists and indeed have been shown to antagonize the Ah-R mediated responses (*11*).

Biomagnification Factors. BMF values for mink liver were estimated for most of the PHHs (eq 2) and normalized to feed consumption (0.22 g of food (g of mink)$^{-1}$ d^{-1}, eq 3) (Table 5). The BMFs were consistent among treatment groups with the exception of those determined in the control group. In the control group, all of the BMFs for the PCDDs and PCDFs were based on concentrations in which one or both of the values were between the limit of detection (LOD) and the limit of quantitation (LOQ).

BMF values for mink livers, in general, increased for PHHs with greater degrees of chlorine substitution (Table 5). The exceptions to this rule were those PHHs that are known to be metabolized, such as 2,3,7,8-tetrachlorodibenzofuran (TCDF) and 3,3′,4,4′-PCB (PCB 77). Both TCDF and PCB 77 had no biomagnification potential in mink based on the results of this study. The BMF for TCDF was less than 1.0, due to its ability to be metabolized in mammals (*40, 41*). Metabolism of TCDF in fishes is not as great as warm-blooded vertebrates (*42*); thus, it is accumulated in fish. Similarly, PCB 77 is also metabolized in mammals (*11*), which is probably the reason the BMF was less than 1.0 in mink livers from this study. BMFs of other PCDF congeners based on the 40% carp treatment group ranged from 27.5 for 1,2,3,4,6,7,8-HPCDF to 75.8 for 2,3,4,6,7,8-HXCDF (Table 5). BMFs of the non-ortho-PCB congeners 3,3′,4,4′,5-PCB (PCB 126) and 3,3′,4,4′,5,5′-PCB (PCB 169) were 12.4 and 15.9 in the 40% carp treatment group, respectively. The concentrations of PCB 126 in the control diet were above the LOQ (Tables 1, 4, and 5), and the BMF for PCB 126 in the control diet group was similar to those of the carp treatment groups (Table 5).

TABLE 5

Normalized Biomagnification Factors (BMFs) for PHHs from Diets to Mink Livers[a]

	BMF				
compound	control	10% carp	20% carp	40% carp	
2,3,7,8-TCDD	1.6*	11.1	11.5*	10.9	
1,2,3,7,8-PECDD		3.5*	6.2	6.4	
1,2,3,4,7,8-HXCDD				9.3*	
1,2,3,6,7,8-HXCDD			26.4*	33.5	
1,2,3,7,8,9-HXCDD	2.6*			15.5*	
1,2,3,4,6,7,8-HPCDD	15.1*	49.8*	49.0*	45.2	
OCDD	8.8*	50.4	62.5*	74.2	
2,3,7,8-TCDF			0.4*	0.4*	
1,2,3,7,8-PECDF					
2,3,4,7,8-PECDF	2.9*		55.0*	54.1	
1,2,3,4,7,8-HXCDF	1.0*		50.1*	64.4	
1,2,3,6,7,9-HXCDF			49.9*	54.9	
1,2,3,7,8,9-HXCDF					
2,3,4,6,7,8-HXCDF				75.8	
1,2,3,4,6,7,8-HPCDF			19.7*	27.5	
1,2,3,4,7,8,9-HPCDF					
OCDF				43.3*	
3,4,4′,5-TCB (81)		1.7*	0.8*	1.0	
3,3′,4,4′-TCB (77)		0.2	0.1*	0.1	
3,3′,4,4′,5-PeCB (126)	15.1	14.5	8.4	12.4	
3,3′,4,4′,5,5′-HxCB (169)	21.4*	12.5	12.4	15.9	
2′,3,4,4′,5-PeCB (123)	1.3	0.4	0.5	0.8	
2,3′,4,4′,5-PeCB (118)	3.4	3.6	4.3	5.9	
2,3,4,4′,5-PeCB (114)	3.7	3.8	3.6	4.7	
2,3,3′,4,4′-PeCB (105)	3.8	4.8	4.6	6.8	
2,3′,4,4′,5,5′-HxCB (167)	4.5	5.9	5.2	7.2	
2,3,3′,4,4′,5-HxCB (156)	5.5	9.2	8.2	11.6	
2,3,3′,4,4′,5′-HxCB (157)	5.6	12.1	11.0	15.4	
2,3,3′,4,4′,5,5′-HpCB (189)	6.3	14.4	6.7	8.9	
total PCBs	3.9	2.4	2.3	3.0	

[a] BMFs normalized to an average consumption of 0.22 g of food (g of mink)$^{-1}$ day^{-1}. Values with an asterisk (*) were derived from concentration data in which one or both values are >LOD but <LOQ. No BFM was reported when both liver and diet concentrations were <LOD.

$\bar{X}$
1.2
0.1
12.6
15.6
0.8
4.3
4.0
5.0
5.7
8.6
11.0
9.1
$\bar{X} = 2.9$

The mono-ortho-PCBs and total PCBs were present in great enough amounts to allow calculation of BMF values for all compounds in all treatments. Again, the BMFs for these were consistent among diets (Table 5). The BMF for total PCBs (2.3–3.9) was similar to those that have been reported in the literature, 2.35–3.0 reported by Wren et al. (*16*) and 2.08–3.36 reported by Platonow and Karstad (*13*). Hornshaw et al. (*43*) reported BMFs from diets to adipose tissues, which when normalized to lipid content (assuming 9% lipid in the diet and 90% lipid in the adipose) were 1.65–2.85. All of these BMFs for PCBs from the various studies were similar to values derived in this study.

The fact that the liver BMF values for the various PHHs were similar across the treatment groups suggests that the mink were at equilibrium with their diets. A concentration dependence of the liver BMF would have suggested that an equilbrium had not been attained. BMF values used in risk assessment are often based on whole body concentrations of the chemical. Our analysis of liver tissues, and hence BMF calculations was based on the toxicological importance of this organ. However, this should not limit the utility of these BMF values in risk assessment, because of the apparent equilibrium that the mink were in with their diets and because the tissue-specific distribution patterns in mustelids are not thought to be great. Leonards and co-workers (*44*) found the distribution patterns of PCBs

TABLE 6

Reproductive Effects in Mink Fed Various Percentages of Carp from Saginaw Bay, MI[a]

	diet			
	control	10% carp	20% carp	40% carp
gestation period (d)	64.5 (1.7)^{A}	58.7 (1.4)^{A}	55.2 (1.3)^{A}	58.7 (1.8)^{A}
no. of live kits whelped	5.0^{A}	3.8^{A}	4.8^{A}	0.7^{B}
(no. of female whelping				
kit body weights (g)				
birth	10.5 (0.2)^{A}	9.8 (0.3)^{AB}	8.7 (0.3)^{BC}	7.5 (0.5)^{C}
3 weeks	98.7 (1.9)^{A}	66.1 (9.8)^{B}	65.8 (4.8)^{B}	
6 weeks	247.9 (19.1)^{A}	197.4 (16.2)^{B}	100.5 (0.2)^{B}	
kit survival (%)				
birth	88	72	83	20
3 weeks	85	31	29	0
6 weeks	85	28	11	0

[a] Mean values followed by standard error of the mean from Heaton et al. (*21*). Values with different letters are significantly different from the others in the same row ($p < 0.05$).

TABLE 7

Mink Reproductive NOAEL, Estimated Threshold Dose, and LOAEL for TEQs and H4IIE TCDD-EQs[a]

	NOAEL	threshold dose	LOAEL
dietary TEQ concn (pg/g)	0.3	1.9	12.6
dietary H4IIE TCDD-EQ concn (pg/g)	1	4.4	19.4
cumulative TEQ dose (ng/mink)	6.6	39.0	231.0
cumulative H4IIE TCDD-EQ dose (ng/mink)	22.3	89.0	355.4
ng of TEQ mink,$^{-1}$ day^{-1}	0.08	0.46	2.75
ng of H4IIE TCDD-EQ mink^{-1} day^{-1}	0.27	1.07	4.23
ng of TEQ kg of body wt^{-1} day^{-1}	0.08	0.42	2.24
ng of H4IIE TCDD-EQ (kg of body wt)$^{-1}$ day^{-1}	0.27	0.96	3.44
liver TEQ concn (pg/g)	11	60	324
liver H4IIE TCDD-EQ concn (pg/g)	<10	70	495

[a] NOAEL based on control group; LOAEL based on 10% carp diet; and estimated threshold dose based on geometric mean of NOAEL and LOAEL.

in the liver, fat, and kidneys of polecats (*Mustela putorius*) to be similar. Therefore, the BMF values from this study derived from lipid-normalized liver concentrations are not likely to differ from BMF values estimated from whole body concentrations.

Reproductive Toxicity. Reproductive toxicity was observed in all of the carp treatment groups as compared to the mink on control diets. The details of these effects were presented in Heaton et al. (*21, 27*) and summarized here (Table 6). There were no significant differences in length of gestation or number of females whelping among treatments, and only in the 40% carp diet was there a significant decrease in the number of live kits whelped per female. Reduced kit body weights at 3 weeks of age occurred in the 10% carp diet and were followed by reduced survival of the kits at 3 and 6 weeks of age (Table 6). Therefore, the lowest observed adverse effect level (LOAEL) in this study was 10% Saginaw Bay carp and the no observed adverse effect level (NOAEL) was the control diet in this study (Table 7). The estimated threshold dose (ETD) for reproductive effects was calculated as the geometric mean of the NOAEL and the LOAEL. When calculated from TEQs or TCDD-EQs, the ETD dietary concentrations are 1.9 or 4.4 pg/g, respectively (Table 7). The mink dietary consumption ETD to protect against reproductive toxicity based on TEQs was 0.42 ng (kg of body wt)$^{-1}$ d^{-1}, and the ETD based on TCDD-EQ was 0.96 ng (kg of body wt)$^{-1}$ d^{-1}. Although a factor of 2 may certainly be biologically important, this amount of uncertainty is fairly small relative to the large amount of uncertainty associated with other components of the risk assessment process. The tissue-based ETDs for reproductive effects in mink were virtually identical whether calculated by TEQs or TCDD-EQs in the mink liver, 60 or 70 pg/g, respectively. If one assumes that either of these measures of Ah-R mediated potency is an accurate representation of TCDD-like toxicity, the sensitivity of mink toward TCDD-induced reproductive toxicity is greater than most, if not all, other species that have been tested (*45*).

The most commonly used and accepted set of TEF values for risk assessment are the international TEF values (I-TEF; *23, 24*). A comparison of TEQs derived from I-TEFs with H4IIE TCDD-EQs in the diets reveals a remarkable similarity in the values (Table 8). Therefore, an ETD for mink based on dietary I-TEQs (ETD = 4.8 pg of I-TEQ/g or 1.1 ng of I-TEQ (kg of body wt)$^{-1}$ d^{-1}) was nearly identical to that using the H4IIE bioassay TCDD-EQs (Table 7). The major difference in the two methods of estimating dioxin-like activity of the mixture was the relative contribution of the various components to the calculated TEQs (Tables 2 and 8). The PCBs contributed nearly 80% of the dioxin-like activity based on I-TEF values (Table 8), while they comprised only approximately 20% based on H4IIE TEF values (Table 2). Liver I-TEQs were approximately 65% that of the H4IIE bioassay TCDD-EQs (Table 8). The contribution of PCBs to the total I-TEQs found in the livers of mink fed the carp diets was approximately 65% (Table 8) as compared to <10% when H4IIE TEF values are used (Table 4). The resultant ETD based on liver concentrations was 61 pg of I-TEQ/g, which was again nearly identical to the estimates based on H4IIE bioassay-derived TCDD-EQs or H4IIE TEF-based TEQs (Table 7). Clearly, the relationships among TEQs derived from various TEF values and TCDD-EQ derived from the H4IIE bioassay need further examination to confirm the consistencies observed in this

TABLE 8

I-TEQ Concentrations (pg/g) in Diets and Livers of Mink Fed Diets Containing Carp from Saginaw Bay, Lake Huron, MI[a]

		I-TEQs (pg/g) in diet				I-TEQs (pg/g) in livers			
compound	I-TEF	control	10% carp	20% carp	40% carp	control	10% carp	20% carp	40% carp
2,3,7,8-TCDD	1	0.0	2.0	3.0	7.0	1.5	21.0	33.5	49.5
1,2,3,7,8-PECDD	0.5	0.0	1.0	0.9	2.0	0.0	3.3	5.3	8.3
1,2,3,4,7,8-HXCDD	0.1	0.0	0.2	0.1	0.3	0.0	0.6	1.0	1.5
1,2,3,6,7,8-HXCDD	0.1	0.0	0.2	0.3	0.6	0.8	5.4	7.7	13.0
1,2,3,7,8,9-HXCDD	0.1	0.0	0.1	0.1	0.1	0.3	0.8	0.8	1.0
1,2,3,4,6,7,9-HPCDD	0.01	0.1	0.1	0.1	0.1	1.2	3.3	2.9	3.8
OCDD	0.001	0.0	0.0	0.0	0.1	0.5	2.2	1.9	2.4
PCDD total		0.1	3.6	4.5	10.1	4.2	36.4	52.9	79.5
% total		9.4	16.8	10.7	12.1	23.8	17.6	16.6	14.3
2,3,7,8-TCDF	0.1	0.0	0.3	0.4	1.3	0.2	16.5	32.0	49.0
1,2,3,7,8-PECDF	0.05	0.0	0.1	0.1	0.2	0.0	1.7	3.7	6.3
2,3,4,7,8-PECDF	0.5	0.0	1.8	3.0	7.0	0.0	12.3	24.3	35.5
1,2,3,4,7,8-HXCDF	0.1	0.0	0.1	0.2	0.3	0.0	0.2	0.2	0.2
1,2,3,6,7,8-HXCDF	0.1	0.0	0.1	0.1	0.2	0.0	3.7	6.0	9.8
1,2,3,7,8,9-HXCDF	0.1	0.0	0.0	0.0	0.0	0.4	3.3	5.8	8.9
2,3,4,6,7,8-HXCDF	0.1	0.0	0.1	0.1	0.2	0.0	0.2	0.2	0.2
1,2,3,4,6,7,8-HPCDF	0.01	0.0	0.0	0.0	0.1	0.0	0.3	0.1	0.3
1,2,3,4,7,8,9-HPCDF	0.01	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
OCDF	0.001	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
PCDF total		0.0	2.4	4.0	9.2	0.6	38.0	72.1	110.1
% total		0.1	11.2	9.4	11.0	3.4	18.4	22.7	19.9
2,3,3',5-TCB (81)	NA[b]								
3,3',4,4'-TCB (77)	0.0005	0.0	0.2	0.3	0.6	0.0	0.0	0.1	0.1
3,3',4,4',5-PECB (126)	0.1	0.5	8.8	21.0	41.0	11.5	121.0	171.5	327.5
3,3',4,4',5,5'-HXCB (169)	0.01	0.0	0.1	0.1	0.2	0.7	0.7	1.2	2.1
non-ortho-PCB total		0.5	9.0	21.4	41.8	12.2	121.7	172.8	329.7
% total		56.8	42.4	50.7	50.0	68.3	58.8	54.3	59.5
2',3,4,4',5-PECB (123)	0.0001	0.0	0.1	0.2	0.3	0.0	0.5	0.8	1.4
2,3',4,4',5-PECB (118)	0.0001	0.2	3.5	6.9	12.5	0.3	5.4	10.5	18.1
2,3,4,4',5-PECB (114)	0.0005	0.0	0.6	1.2	2.3	0.4	3.2	5.6	9.3
2,3,3',4,4'-PECB (105)	0.0001	0.1	1.2	2.3	4.1	0.1	1.2	2.3	3.7
2,3',4,4',5,5'-HXCB (167)	0.00001	0.0	0.0	0.0	0.0	0.0	0.0	0.1	0.1
2,3,3',4,4',5-HXCB (156)	0.0005	0.1	0.7	1.4	2.5	0.0	0.6	1.3	2.1
2,3,3',4,4',5-HXCB (157)	0.0005	0.0	0.1	0.3	0.5	0.0	0.0	0.0	0.0
2,3,3',4,4',5,5'-HXCB (189)	0.0001	0.0	0.0	0.0	0.1	0.0	0.0	0.0	0.0
mono-ortho-PCB total		0.3	6.3	12.4	22.4	0.8	10.9	20.6	34.8
% total		33.7	39.6	29.3	26.8	4.6	5.3	6.5	6.3
grand total I-TEQs		0.9	21.2	42.2	83.5	18	207	318	554
H4IIE TCDD-EQs		1.0	19.4	40.0	80.8	<10	495	439	656

[a] I-TEF values for PCDD/Fs (*23*) and PCBs (*24*). [b] NA, not assessed.

study. This is particularly true as attempts are made to understand the relative importance of known or measured PHHs (i.e., PCBs, PCDDs, and PCDFs) and to predict the contribution of unknown or unmeasured PHHs. The H4IIE bioassay is an integrative tool and may most accurately assess the toxicity of complex biological systems when it is calibrated for the response of that system.

Regardless of the method of determination, TEQs from an additive toxicity model or H4IIE bioassay, or whether they were based on liver tissue or dietary concentrations, the ETD values for the protection of mink reproductive health were similar. A recent review of mink reproductive toxicity caused by technical PCB mixtures (*46*) estimated that the tissue concentration of TEQs (whole body) that results in 50% kit survival was 200 pg/g, while the dietary threshold was estimated to be 17 pg/g using the TEFs of Safe (*11*). The current model for the protection of mink health in the Great Lakes comes from the Great Lakes Water Quality Initiative (GLWQI; *47*). The GLWQI estimates a NOAEL for TCDD of 0.1 ng (kg of body wt)$^{-1}$ d^{-1} (*47*). According to our study, this amount of TCDD or total dioxin-like activity in the diet should be safe for mink reproduction. The major shortcoming of the assessment procedure of the GLWQI is that only one contaminant, TCDD, is considered, while it can be seen from our analysis that TCDD only accounts for a small portion of the dioxin-like potency in this Great Lake fish sample. An additive model is needed for this set of compounds.

Conclusions

Dioxin-like potency of the PHH mixtures largely followed an additive model of toxicity as compared with the H4IIE bioassay. Consistent dietary and liver tissue-based threshold concentrations for reproductive toxicity in mink were estimated regardless of whether PHHs were quantified as TEQs (additive toxicity) or TCDD-EQs (H4IIE bioassay). Consumption-normalized mink liver BMFs were consistent among measured values and treatment groups and may be used in exposure assessments for field-collected mink. Based on TEQs or TCDD-EQ, mink are among the most, if not the most, sensitive mammalian species to the reproductive toxicity of TCDD and Ah-R agonists.

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